Proposed Decision Memo for Lumbar Artificial Disc Replacement (CAG-00292N)

Decision Summary

The Centers for Medicare and Medicaid Services (CMS) is seeking public comment on the proposed determination that the evidence is not adequate to conclude that lumbar artificial disc replacement with the Charite lumbar artificial disc is reasonable and necessary. Therefore, we propose to issue a national noncoverage determination.

We are requesting public comments on this proposed determination pursuant to Section 731 of the Medicare Modernization Act. We are particularly interested in comments that include evidence we did not review or that assess how we evaluated the evidence included. After considering the public comments and any additional evidence we will make a final determination and issue a final decision memorandum.

Back to Top

Proposed Decision Memo

TO: Administrative File: (CAG-#00292N)
Lumbar Artificial Disc Replacement

FROM:

Steve Phurrough, MD, MPA
Director
Coverage and Analysis Group

Marcel E. Salive, MD, MPH
Director
Division of Medical and Surgical Services

Deirdre O'Connor
Lead Health Policy Analyst, Division of Medical and Surgical Services

Jyme Schafer, MD, MPH
Lead Medical Officer, Division of Medical and Surgical Services

Shamiram Feinglass, MD, MPH
Medical Officer, Division of Items and Devices

SUBJECT: Proposed Coverage Decision Memorandum for Lumbar Artificial Disc Replacement
DATE: February 15, 2006

I. Proposed Decision

The Centers for Medicare and Medicaid Services (CMS) is seeking public comment on the proposed determination that the evidence is not adequate to conclude that lumbar artificial disc replacement with the Charite lumbar artificial disc is reasonable and necessary. Therefore, we propose to issue a national noncoverage determination.

We are requesting public comments on this proposed determination pursuant to Section 731 of the Medicare Modernization Act. We are particularly interested in comments that include evidence we did not review or that assess how we evaluated the evidence included. After considering the public comments and any additional evidence we will make a final determination and issue a final decision memorandum.

II. Background

Millions of Americans suffer from pain related problems (Salovey, Seiber et al. 1992). Low back pain is a common condition, with sixty to eighty percent of U.S. adults afflicted at some time during their life (U.S. Preventive Services Task Force 1996). Low back pain can be defined as symptoms of pain, muscle tension, or stiffness localized below the costal margin and above the inferior gluteal folds, with or without leg pain (Manek, MacGregor 2005). Low back pain can be thought of as being either nonspecific or specific. In specific types of low back pain, the symptoms are caused by pathological conditions such as spinal fractures, cancer, or infection and can be identified and treated appropriately (Manek, MacGregor 2005). Approximately 90% of low back pain is of the nonspecific type (Manek, MacGregor 2005). In nonspecific low back pain, most patient's symptoms resolve satisfactorily within a relatively short time span. In the 5 – 10% of patients whose pain does not satisfactorily resolve, the symptoms can be disabling. Some psychosocial risk factors for the progression to chronicity have been identified (Manek, MacGregor 2005). In general, the social and economic impact of chronic pain is enormous (Salovey, Seiber et al. 1992).

Discovering the cause for nonspecific low back symptoms remains challenging. Haldeman states "…we do not know the origin of low back pain in the majority of cases…" and attributes this conundrum to the unique anatomic complexity of the spine (Haldeman 1999). Neurophysiologic mechanisms of pain sensation are poorly understood, adding to the difficulty in localizing the pain source (Haldeman 1999). Frequently, persistent low back pain is attributed to a damaged intervertebral disc, which bears some of the highest loads in the human body and is almost avascular (Huang, Sandhu 2004). Disc damage, or degeneration, can occur as an ongoing process where ultimately the disc's reparative capacity is overwhelmed, leading to continued changes. Huang and Sandhu stated, "it is not surprising that DDD [degenerative disc disease] is a common phenomenon in middle age and a universal condition in old age." While from a simple mechanical aspect it could be hypothesized that DDD is a cause for pain, disc degeneration is also observed in individuals without pain (Boden, David et al. 1990).

Initial treatment of pain believed to be caused from degenerative disc disease is conservative care. Conservative care can include physical therapy, manipulation, massage, pain medications, and exercise. The majority of patients will have acceptable results with a non-surgical approach. When patients fail conservative care, surgery becomes an option. Until recently in the United States, surgical options available for degenerative disc disease have ranged from discectomies (open or microsurgical) to percutaneous nucleotomies, chemical and thermal nucleolysis and/or spinal fusion (Gibson, Wassell 2005). Spinal fusion has been the predominant surgical treatment for degenerative disc disease (DDD) that does not respond to other treatments. Fusion proposes to relieve pain by eliminating motion in the area of the disc space and/or by disc mechanical load reduction. Nevertheless, the indications for lumbar spinal fusion are variable and not clearly defined (Krismer 2002). These different opinions concerning the indications for back surgery are reflected in the significant regional variation of rates of surgery, surgical techniques used, technical success and rate of fusion (Gibson, Wassell 2005). Satisfactory clinical outcomes can range from 16 to 95% (Gibson, Wassell 2005). Short term relief of pain may perhaps occur with the various types of fusion procedures, but long-term results remain controversial (Bertagnoli, Kumar 2002). Suspected problems include accelerated degeneration of the adjacent lumbar segments, psuedoarthrosis, spinal stenosis and persistent or recurrent low-back pain. In an attempt to overcome these potential long-term problems, the idea of a total artificial disc replacement as a treatment for pain believed secondary to degenerative disc disease has been proposed as an alternative to spinal fusion. As possible added benefits, it has been postulated that total disc replacement may have a protective role on the facet joints, and restore lumbar segment motion (Bertagnoli, Kumar 2002). The artificial disc concept is not new. In the late 1960's, Fernstrom explored the possibility of replacing the intervertebral disc with an artificial disc. Much research and development work has been done since then. The current SB Charite disc is the third modification of a device first developed in 1982 by Buttener-Janz and Schellnack at the Charite Clinic in the former East Germany. There are other artificial discs in use in other countries and additional disc implants under development. Intervertebral disc replacement design has been problematic due to the three-column structure of the spine, and the three separate joints at each level. The disc is not a true joint, and functions in both mobility and damping, with the center of rotation moving constantly along three axes (Gunzburg, Mayer et al. 2002). Huang and Sandhu suggest the ideal disc replacement would perform the functions of the replaced native disc, which include preservation of physiologic range of motion, transmission of compressive loads across the disc space, protection of the posterior elements (facets) from abnormal loads, and then to function for many years. The current replacement discs that are either approved or under study in the US have metal endplates that affix to the vertebral bony endplates with some mechanism between these two plates that allows for motion in various planes. The Charite disc has an ultra high molecular weight polyethylene insert that sits between the two metal endplates. The metal endplates have external spikes for engagement of the device into the vertebral bony endplates. Components come in various sizes for a close fit to the patient's anatomy. The motion of this disc is thought to be minimally constrained in flexion, extension, lateral bending, and axial rotation. It is constrained in compression. The other disc implants in development in the United States are somewhat similar but can vary in material (metal on polymer or metal on metal), motion design, and method of fixation to vertebral endplate (Santos, Polly et al. 2004). Anderson and Rouleau offered, "The current designs are diverse and, thus far, the effects of their individual characteristics on results are unknown." As of 2004, more than 7,000 patients worldwide had been implanted with the Charite disc (FDA in-depth statistical review for expedited PMA 2004).

The surgical procedure for disc replacement involves an anterior approach for exposure of the spine. With this approach, complications of vessel injury can occur and have the potential to be life threatening (Santos, Polly et al. 2004). On revision surgery, Santos, et al., state, "Revision surgery for a failed disc arthroplasty is life threatening. Dealing with the scarring around the great vessels is the main challenge. Indeed, the location of vital vascular structures may make it altogether impossible to perform such anterior abdominal exposures." Other postoperative difficulties such as infection, persistent pain, instability, and osteolysis can occur (Santos, Polly et al. 2004).

In general, the cost benefit of surgery for degenerative disc disease is not without question. The 2005 Cochrane review of surgery for degenerative lumbar spondylosis provides, "There is no good evidence on cost-effectiveness" (Gibson, Wassell 2005). Concern about cost benefit has been expressed for the artificial disc in particular. Within 5 years of its release, it is predicted that spinal arthroplasty (lumbar and cervical) could reach an annual cost of $2.18 billion in the United States, with the suggestion by Singh that this estimate is conservative (Singh, Vaccaro et al. 2004). Santos stated, "…long-term clinical outcome using validated instruments are necessary to justify the added cost of these procedures,"(Santos, Polly et al. 2004).

III. History of Medicare Coverage

Medicare does not currently have a national coverage determination (NCD) on lumbar artificial disc replacement. When there is no NCD in place, coverage for the procedure is overseen by local Medicare contractors.

Current Request

On August 16, 2005, CMS accepted a request from Richard A. Deyo, M.D., for an NCD on the CHARITE-Lumbar Artificial Disc Replacement for non-coverage. Dr. Deyo had a concern that, "the Charite disc is a new technology whose real place in spine therapy remains to be determined," and that important scientific evidence generalizing safety and effectiveness is not available.

CMS is evaluating lumbar artificial disc replacement with a focus on the CHARITE Lumbar Disc in this analysis, since this was the only disc implant that had FDA approval at the time this proposed decision memorandum was ready for posting. However, we anticipate that when another lumbar spinal disc implant receives approval from the FDA that CMS will, by external request or internal direction, open this NCD for reconsideration with a thorough review of the evidence.

Benefit Category

Medicare is a defined benefit program. An item or service must fall within a benefit category as a prerequisite to Medicare coverage. §1812 (Scope of Part A); §1832 (Scope of Part B); §1861(s) (Definitions of Medical and Other Health Services). Charite Lumbar Artificial Disc Replacement would be eligible for coverage under §1861(q), physicians services and §1861(b) inpatient hospital services.

IV. Timeline of Recent Activities

August 5, 2005	Dr. Richard A. Deyo submitted a letter formally requesting an NCD on the CHARITE-Lumbar Artificial Disc Replacement for non-coverage.
August 16, 2005	CMS opened the NCD process pursuant to Dr. Deyo's request. A tracking sheet was posted on the web site and the initial 30 day public comment period commenced.
September 12, 2005	Meeting with DePuy Spine.
September 16, 2005	The initial 30 day public comment period ended.

V. Food and Drug Administration (FDA) Status

The FDA approved the CHARITE™ Artificial Disc in October of 2004 (http://www.fda.gov/cdrh/pdf4/p040006.html).

The CHARITE™ Artificial Disc is indicated for spinal arthroplasty in patients who are skeletally mature, have degenerative disc disease at one level in the lumbar spine from L4 to S1, have no more than 3 mm of spondylolisthesis at the involved level, and have had no relief from pain after at least six months of non-surgical treatment. It is an artificial intervertebral disc made from metal and plastic that is used during a spinal arthroplasty to replace a diseased or damaged intervertebral disc and also treat pain associated with degenerative disc disease.

VI. General Methodological Principles

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve net health outcomes for patients. An improved net health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A. In general, features of clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, and the blinding of readers of the index test, and reference test results.

Public comment sometimes cites the published clinical evidence and gives CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction

A summary of the evidence used to arrive at the proposed determination is provided. This summary represents the evidence relating to the treatment of pain from degenerative disc disease with lumbar artificial disc replacement and includes a clinical trial, case series reports, and technical reviews. The evidence CMS examines has as its focus health outcomes, or, the benefits and harms of a particular treatment. Outcomes that are usually heavily weighted by CMS - morbidity and mortality - are difficult to examine in the context of treatment for chronic low back pain which is a symptom, not a disease. In chronic low back pain, sustained improvement in pain perception and a reduction in the pain-related functional restriction are generally the focus of study outcomes. Measuring a reliable improvement in chronic pain is problematic as pain is subjective and is particularly responsive to the placebo effect; therefore, clinical trials with appropriate controls utilizing independently assessed validated instruments are most heavily weighted. The measurement of treatment effect for low back pain has shifted from physician-based assessment (with outcomes of excellent, good, fair, and poor) to a patient-based self-report of pain and disability (Hagg, Fritzell et al. 2003).

Treatment effect in chronic low back pain is measured with patient-based, multi-item instruments. Two instruments validated for measurement of back pain are commonly used in the assessment of low back pain from degenerative disc disease (Hagg, Fritzell et al. 2003).

The Oswestry Disability Index (ODI) is a condition specific outcome measure used in the management of spinal disorders. The measure is an indication of the extent to which a person's functional level is restricted by pain. The other commonly used measure in chronic back pain treatment effect is the visual analogue scale (VAS), which is a method to assess pain intensity. With the use of these instruments for measurement, a consideration must be given to the clinical meaning of a change in the score (or, for a change in instrument score to be clinically meaningful the patient should experience a change in how he feels or functions). Other considerations include the error of measurement of the instrument used and the clinical importance of a statistically significant score change. In a study by Hagg, et al., of 289 patients treated surgically or non-surgically in a randomized controlled trial, the standard error of measurement of the ODI was 4 units, with a 95% tolerance interval of 10, and the minimum difference that appeared clinically important of 10 units. The minimal clinically important difference of VAS back pain was 18 – 19 units with a 95% tolerance interval of 15. It was interesting to note that in this study, improvement after treatment tended to occur to a greater extent in sleep disturbance, ability to do usual things and psychological irritability, but to a lesser extent in the ability to sit, stand and lift. The FDA has chosen a minimum 15-point change in ODI for spinal surgery patients as a clinically meaningful difference (FDA CDRH Orthopedic and Rehabilitation Devices Panel Meeting, 2005).

Some investigators have used the Stauffer Coventry classification, or some modification thereof to measure results. The criteria for clinical results for the Stauffer and Coventry classification are provided in Table 1 (Sott, Harrison 2000).

Table 1

Pain relief (%)	Return to work	Physical restriction	Use of analgesics
Good 76 – 100	Yes	No or slight	No
Fair 26 – 75	Yes, with limitations	Yes, limited activities	Frequent (mild)
Poor < 25	No, disabled	Yes, greatly limited	Regular (strong)

Additionally, other quality of life measures are sometimes used. The SF-36 Health Survey, a 36 question form that measures general health status, can be used. Of the 8 health profiles that are included in this survey, only one or two components may be reported, such as the physical functioning composite score or the mental health composite score.

Physiologic segmental mobility is viewed as an important design feature of the artificial disc. Some studies have reported range of motion as an outcome. With fusion, there is reduced motion at the fused segment. The FDA has defined fusion as < 5 degrees of angular motion (FDA guidance document 2000). The theoretical mobility provided by the artificial disc has yet to directly correlate to a proven benefit in how the patient feels or functions, making the clinical significance of post treatment range of motion unclear. Therefore, CMS does not consider post treatment range of motion an important clinical outcome of interest in this memorandum.

Well designed clinical trials can provide the strongest evidence for treatment effect. Clinical trials can be designed to show superiority, a priori, where the superior clinical performance of the investigational agent as compared to the control agent is anticipated. When the investigational agent is believed to have comparable efficacy to the control, but has other advantages, for example fewer adverse events or less cost, a noninferiority trial is an option. In a noninferiority trial, the aim is to demonstrate that the investigational agent is not worse than the control by a certain pre-specified margin, referred to as the delta. In the statistical approach for noninferiority analysis, the delta is compared with the one-sided 95% confidence interval for the difference between the success rate point estimates of the investigational agent and control. If the lower bound of this one-sided confidence interval is less than the delta, then the statistical definition of noninferiority is met.

B. Discussion of evidence

1. Question:

The development of an assessment in support of Medicare coverage decisions is based on the same general question for almost all requests: "Is the evidence sufficient to conclude that the application of the item or service under study will improve net health outcomes for Medicare patients?" For this NCD, the question of interest is:

Is the evidence sufficient to conclude that lumbar artificial disc replacement with the Charite lumbar artificial disc will improve net health benefits for low back pain due to degenerative disc disease in the Medicare population?

2. External technology assessment

CMS did not commission an external technology assessment.

3. Internal technology assessment

CMS performed an extensive literature search utilizing PubMed for new randomized controlled trials (RCTs) and systemic reviews evaluating the use of lumbar artificial disc replacements for the treatment of degenerative disc disease. The literature search was limited to the English language and specific to the human population, but included studies conducted in all countries, including the United States (see evidence tables in Appendix B). Public access information from the FDA website was also used.

Evidence for the Charite lumbar artificial disc came from the FDA Premarket Approval Application clinical trial, several case series reports, a systematic review, and adverse events reported to the FDA's Manufacturer and User Facility Device Experience (MAUDE) database**.**

Evidence Summary

Charite Clinical Trial

In 2005, Blumenthal and McAfee (in two articles) published results of the clinical trial of the SB Charite III disc compared to the BAK interbody fusion device that led to FDA approval in October, 2004 (Blumenthal, McAfee et al. 2005; McAfee, Cunningham et al. 2005). The investigators' purpose was to compare the safety and effectiveness of lumbar total disc replacement, using the Charite disc, with anterior interbody fusion, for the treatment of single-level degenerative disc disease from L4-S1, unresponsive to nonoperative treatment for at least 6 months prior to enrollment. The trial enrolled 375 patients at 14 centers across the United States. The inclusion criteria included: 1) age 18 to 60 years; 2) symptomatic DDD confirmed by discography; 3) single-level DDD at L4-L5 or L5-S1; 4) Oswestry score $\geq$ 30; 5) VAS score $\geq$ 40 (of 100); 6) failed $\geq$ 6 mos of appropriate non-operative care; 7) back and/or leg pain with no nerve root compression; 8) able to tolerate anterior approach; 9) able and willing to comply with follow-up schedule; 10) willing to give written informed consent. Exclusion Criteria included the following:

- Previous thoracic or lumbar fusion,
- Current or prior fracture at L4, L5, or S1,
- Symptomatic multilevel degeneration,
- Noncontained herniated nucleus pulposus,
- Spondylosis,
- Spondylolisthesis > 3 mm,
- Scoliosis > 11°,
- Mid-sagittal stenosis < 8 mm,
- Positive straight leg raise,
- Spinal tumor,
- Osteoporosis, osteopenia, or metabolic bone disease,
- Infection,
- Facet joint arthrosis,
- Psychosocial disorder,
- Morbid obesity,
- Metal allergy,
- Use of a bone growth stimulator,
- Participation in another study,
- Arachnoiditis,
- Chronic steroid use,
- Autoimmune disorder,
- Pregnancy, or
- Other spinal surgery at affected level (except discectomy, laminotomy/ectomy, without accompanying facetotomy or nucleolysis at the same level to be treated).

Five patients at each location (71 total patients) received disc replacement before randomization, which was provided for in the protocol as the opportunity to "insure technical competence with the treatment procedure." Patients were randomized in a 2:1 ratio (treatment: control), stratified by site in blocks of six. Allocation concealment was done with sequentially numbered envelopes that were opened before surgery, so investigators, staff, and patients were blinded up until this point. Of the randomized patients, 205 patients received the Charite disc replacement and 99 received the BAK cage fusion. Control and treatment groups did not differ statistically on gender, age, race, height, previous spinal surgery, and pre operative work status, but did vary on weight (treatment mean 77.5 kg [SD 15.67], control mean 81.7 kg [SD 16.46], p = 0.0349), with body mass index being borderline significant (26 [SD 4.23], control 27 [SD 4.76], p = 0.0557). The control group received anterior fusion with BAK threaded fusion cages packed with iliac crest autograft. The statistical hypothesis was one of noninferiority, or equivalence, to BAK fusion, where equivalence was defined such that the success rate of Charite was no worse than that of BAK by a pre-specified delta of 15% in the investigator's protocol. Data were collected at regular intervals up to 24 months post procedure through the trial end and included the ODI, VAS, SF -36 scores, and radiographic information. In a publicly accessible FDA document, concomitant disease of the participants is mentioned as is pre-operative activity (FDA in-depth statistical review for expedited PMA 2004).

Table 2

Baseline evaluation	Charite	BAK	p-value *
Normal Activity level Before back injury Active Moderate Light Minimal	 167 (92%) 13 (7%) 1 (1%) 1 (1%)	 73(86%) 10 (12%) 2 (2%) 0	 0.23
Pre-operative Activity Active Moderate Light Minimal	 9 (5%) 25 (14%) 48 (26%) 100 (55%)	 0 5 (6%) 23 (27%) 57 (67%)	 0.02
Concomitant Disease (> 3%) Hypertension Asthma Hepatitis Osteoarthritis Anemia Peptic Ulcer Cancer Other	 15 (8%) 11 (6%) 5 (3%) 7 (4%) 6 (3%) 6 (3%) 2 (1%) 80 (44%)	 12 (14%) 6 (7%) 7 (7%) 3 (4%) 4 (5%) 3 (4%) 3 (4%) 33 (39%)	
***** Fisher's exact test for categorical variables and t-test for continuous variables			

Clinical success was judged in terms of a composite outcome that required these four criteria to be met:
1. Improvement in the ODI of at least 25% at 24 months as compared to baseline,
2. No device failures requiring revision, reoperation or removal,
3. Absence of major complications, defined as major blood vessel injury, neurologic damage, or nerve root injury, and
4. Maintenance or improvement in neurological status at 24 months, with no new permanent neurological deficits compared to baseline.

Patient accountability from the Blumenthal article and the FDA summary of safety and effectiveness data is reported in Table 3 (FDA Summary of Safety and Effectiveness Data 2004).

Table 3

	12 months		24 months	
Patients	**Charite**	**Control**	**Charite**	**Control**
Randomized	205	99	205	99
Deaths	1	0	1	0
Failures	7	4	12	8
Withdrawn	5	9	16	17
Expected	192	86	176	74
Missed	8	5	15	8
Actual	184	81	161	66
Note: failures include device removals, revisions, and supplemental fixations. Expected = randomized patients – deaths – failures – withdrawn. Missed are those patients who were "out of the window" of the protocol.				

No statistical analysis plan was in the original protocol documents (FDA in-depth statistical review for expedited PMA 2004). The 71 patients that were regarded as training patients were not included in this analysis. Using the composite measure for clinical success, the artificial disc had an overall success rate reported as 57% and the BAK cage had a success rate of 46%, with the noninferior p value listed as 0.0001. Numerators and denominators were not given for these numbers, but this appears to be a strict intention to treat analysis. The FDA requested that the data also be analyzed and reported using: 1) an improvement in the ODI $\geq$ 15 points at 24 months compared to the score at baseline; and 2) a noninferiority margin of 10%. The FDA concluded that "The two-sided confidence interval indicates that the overall success rate for the Charite Artificial Disc is not worse than the control rate by more than 10%, regardless of which set of study success criteria is used" (FDA Summary of Safety and effectiveness data 2004). Though, for the previous analysis the table says "Comparison of Success Rates for Efficacy at 24 months", the number of subjects (completers) was 184 for Charite and 81 for the control, which corresponds to the 12 month completers. Blumenthal, et al., stated, "Sensitivity analysis were performed to evaluate the potential impact of incomplete subjects (e.g., lost to follow-up)." There was no difference between the two groups as far as operative time (111 minutes in the investigational group and 115.3 minutes in the control group, p = 0.562), blood loss (207 cc in the investigational group and 224 cc in the control group, p = 0.6012), or level of implantation. Mean duration of hospitalization did differ; however, discharge criteria were not standardized (investigational 3.7 days [SD 1.8], control 4.2 days [SD 1.99]; p = 0.004).

In both investigational and control arms the VAS and ODI scores improved at all follow-up times compared to baseline ($p < 0.001$ for all times). Changes were more rapid in the Charite group, and the difference between the two groups was statistically significant until the 24 month follow-up for both groups. No conclusions can be made in respect to time to improvement as the study was designed to demonstrate noninferiority at the 24 month time frame only. At 24 months, the mean decrease in ODI in the investigational group (from 51 to 26) as compared to the control group (52 to 33) did not differ significantly ($p = 0.267$); similarly, VAS decrease in the investigational group (from 7.2 to 3.1) as compared to the control group (7.2 to 3.7) did not differ significantly ($p = 0.1074$). For the component SF-36 scores, 99 (73%) Charite patients and 41 (66%) BAK patients had a 15% or greater improvement in the Physical Composite Score (PCS) at 24 months, and 8 (50%) Charite patients and 34 (55%) BAK patients had a 15% improvement for the Mental Composite Score (MCS). These were not statistically different with a $p = 0.345$ and 0.4959, respectively (FDA PMA memorandum Clinical Review 2004).

The adverse events from the FDA clinical review are listed in Table 4 (FDA PMA memorandum Clinical Review 2004). Device failure appeared to be incorporated into the composite clinical success score, but the category in the composite score for major complications was more narrow than the adverse events listed in Table 4 (Blue Cross Blue Shield 2005). Device-related adverse events do not appear to be incorporated into the composite score (Blue Cross Blue Shield 2005). From Table 4, Charite had a higher percentage of patients with severe or life threatening events and device related adverse events; p values were not given.

Table 4*

Adverse Events	Charite disc	BAK cage
Patients with severe or life threatening events	15% (30/205)	9% (9/99)
Device-related adverse events	7.3% (15/205)	4% (4/99)
Device failures	4.9% (10/205)	8.1% (8/99)

*FDA PMA memorandum Clinical Review 2004

At 24 months, many patients who met the criteria of clinical success were using narcotics to control pain. In the patients deemed a success at 24 months, the rate of narcotic usage in the investigational group was 64% (73 of 114) and 80.4% (37 of 46) in the control group. Narcotic usage was not defined and was not given for patients who did not meet the success criteria at the 24 month follow-up.

Follow-up radiographs were obtained, scanned, digitalized, and analyzed by a software program (McAfee, Cunningham et al. 2005). At 24 months, range of motion (ROM) as measured on lateral flexion/extension films was 113.6% of preoperative measure (a 13.6% increase from baseline) in the investigational group and decreased in the control group, as would be expected for fusion. No statistically significant association was found between ROM and success/failure at 24 months for those who had data available to the FDA reviewer (FDA Summary of Safety and effectiveness data 2004). Fusion rate was judged to be 91.9%. At 24 months, 82.9% of both the Charite artificial disc training and randomized subjects were graded as having ideal placement, 10.7% as suboptimal placement, and 6.2% as poor placement. The authors stated that ODI scores at 24 months correlated with the degree of technical accuracy ($p < 0.05$), as did VAS scores ($p = 0.016$). The disc was more effective in restoring height of the collapsed disc space as compared to fusion ($p < 0.05$), and had less subsidence ($p < 0.05$). The authors stated that, "Long-term radiographic follow-up is necessary to determine if TDR can prevent adjacent segment breakdown."

Neurologic status included the following information: reflexes at the knee and ankle; motor function; sensitivity to light touch; strength of lower extremities; and straight leg raise. Neurologic status was reported as equivalent between the investigational group and control group at 6, 12 and 24 months (Geisler, Blumenthal et al. 2004). There was no significant difference between the number of patients with neurological adverse events comparing investigational group (16.6%) to control group (17.2%).

Limited information was provided in the FDA's summary of safety and effectiveness data for the initial training group of 71 patients (FDA Summary of Safety and effectiveness data 2004). There were higher early (within the first 2 days of surgery) adverse events in this group (33 patients, or 46.5%) than in the randomized group (58 patients, 28.3%). The rates at all other time periods were similar between the two groups. There were more device-related adverse events in the training cases (8 events, 11.3%) than in the randomized group (14 events, 6.8%).

Case Series

In 1994, Griffith published a retrospective review of 93 patients (3 surgeons' experience) with 139 Model III Charite implants (Griffith, Shelokov et al. 1994). A single prosthesis was implanted in 53%, two prostheses were in 45%, and 2% received three prostheses. One surgeon provided additional data on 58 earlier design prostheses (Models I and II) that were implanted in 49 patients. The authors analyzed data mainly from those patients implanted with the Model III disc, unless it was noted otherwise. Including all data, average age was 43.0 +/- 7.3 years (range: 25 to 59). For the primary study group, the diagnosis was DDD (65.2%), postnucleotomy syndrome (15.0%), internal disc derangement (10.9%), failed fusion (3.3%), instability (1.2%), and herniated nucleus pulposus (1.2%). Forty-one percent had prior back surgery. Average follow-up was 11.9 +/- 8.3 (n= 90) months (range of 1 to 37 months). Three percent of patients who were implanted with Model III were not followed up or were lost to follow up. If patients had more than one follow-up, the last follow-up visit was used for the analyses. Pain experience was measured using a 10 point analog pain scale for right and left leg pain and back pain. There was improvement in the intensity of pain in all three areas ($p < 0.001$), with a total of 71 patients (one surgeon did not report analog pain scores) included in this analysis. Patients' pain was also judged by qualitative change in pain intensity for these three areas as increased, decreased, or unchanged. Here, also, most patients had an improvement ($p < 0.01$). Neurologic weakness (by physical exam) was present in 21 patients (23%) before the surgery. At the follow-up, 17 of 21 patients no longer presented with neurologic weakness. Similarly, there was a 50% reduction in the number of patients with a positive straight leg raising (SLR) test on follow-up exam (left leg positive SLR: 69% preoperative to 35.5% on follow-up; right leg positive SLR: 63% preoperative to 38.7% on follow-up). A comparison of the patients' ability to walk preoperatively and at the most recent follow-up (n= 71, data was unavailable from one surgeon) showed that 39% improved their self-reported walking distance, 2% decreased their walking distance, and 58% remained the same. Subjective, clinical estimates of lumbar flexion and extension showed an increase in both flexion and extension ($p < 0.01$), though the authors noted that the data should be viewed with caution since they were obtained retrospectively and "were not independently assessed with a validated technique." No statistical difference in work status at follow-up could be detected, though work status results differed between the individual surgeons (p value not given). The authors stated, "Inappropriate choice of prosthetic size resulting in implant migration/subsidence or dislocation occurred in 6.5% of the patients in which Model III was used; the incidence of these complications as a function of the number of prostheses implanted was 4.3%." The reported complications that were related to the procedure, but not necessarily to the device's function, included: phlebitis/leg thrombosis (2), injured vein (6), wound bleeding/dehiscence (2), superficial wound infection (1), muscle atrophy (1), urinary tract infection (4), incontinence (3), constipation/defecation difficulty (4), nausea (1), skin paresthesia (1), hematoma (11), hypotension by blood loss (1), retroejaculation (1), and sympathetic sign in left leg (1). Complications considered by the authors as equivocal included: allergy (1), instability "feeling" (2), new paresthesia (1), unspecified neurologic (2), abdominal, leg, thigh, or lumbar pain (10). The Charite III had 3 re-operations out of 93 patients (3%). The re-operation rate for I and II due to complications of implantation was reported to be 5 of 49 patients (10%).

In 1996, Cinotti retrospectively analyzed the follow-up of 46 patients who had the Charite SB III disc implanted (Cinotti, David et al. 1996). Preoperative diagnosis included disc degeneration in 22 patients and failed disc excision surgery in 24 patients. Thirty-six patients had a single level prosthesis and 10 patients had 2 levels implanted. Post- surgery follow-up ranged from 2 to 5 years, with an average of 3.2 years. The patients had been operated on by one surgeon. Surgery contraindications were degenerative changes of the facet joints identified by CT or MRI, disc degeneration adjacent to a fused area and spondylolisthesis. After surgery, 18 patients wore a corset for 3 months, and 28 patients began exercising within 1 week after surgery (no details). Patients were evaluated by one of the authors who did not participate in the disc replacements. Patients' overall satisfaction, as well as pain sensation, need for analgesics, and the ability to resume work or activities of daily living was reported. Guidelines previously reported by the authors (not detailed in this paper) were used to rate clinical results as excellent, good, fair, or poor.

- Clinical outcome was rated as excellent in 11 patients (24%), good in eighteen (39%), fair in fourteen (30%), and poor in three (7%).
- Patients' satisfaction was reported as a great benefit by 14 patients (30%), a great but not complete benefit by 17 patients (37%), a mild improvement by 12 patients (26%), and no improvement or worsening by three (7%).
- Analgesic drugs were taken occasionally by four patients (9%) and continuously by twelve (26%).
- Resumption of work or daily life activities occurred at the same level in 31 cases (67%) and at a lower level in nine (20%). Four patients, (9%), stated they could not work because of severe back pain and 2 were unemployed.

- Clinical results were rated as satisfactory in 69% of patients (25 of 36) who had single level disc replacement and 40% (4 of 10) in those who had 2 level disc replacement.
- Eight of 17 patients who had unsatisfactory results had a subsequent fusion. Seven of the eight underwent posterolateral fusion with the disc implant left in place, with only three of these patients having satisfactory results at follow-up.

The authors stated, "In the present series, the proportion of satisfactory results (63%) was lower compared with the figures reported for arthrodesis (65 – 90%)." They attributed part of this to the learning curve of the surgery, and that the surgical indications and treatment of patients after surgery changed over time with the surgeon's increasing experience. Two level surgery was discontinued. They further concluded, "The main cause of poor outcomes appear to be an inappropriate selection of patients undergoing disc replacement…". The authors commented on important issues related to the surgical approach; because "the placement of the prosthesis into the disc space needs a larger exposure of the anterior annulus compared with anterior interbody fusion", there is a "greater risk of damaging the big vessels and the sympathetic chain", with mobilization of big vessels carrying a greater risk of complications in elderly patients. The authors reported a complication rate in patients undergoing disc arthroplasty of 19%, with a comparable rate in those who had anterior fusion of 15%. Other complications are also noted. One patient (2%) had an anterior dislocation of the implant, and 9% had subsidence of the prosthesis into the vertebral bodies, attributed to undersizing of the prosthesis. Interestingly, in patients with a malpositioned prosthesis, there often was noted ossification of the intervertebral space. They noted that, "in case of failure of the prosthesis, there is an intrinsic tendency for the motion segment to undergo fusion." There was an average vertebral motion of 9 degrees in the sagittal plane at the operated level, while the authors suggested that the prosthesis should have provided a range of motion of 12- 14 degrees in flexion-extension. It was unclear what this meant clinically. Longer term follow-up was recommended to monitor for prosthesis failure, wear of the materials, and loosening of the implant.

In 1997, Lemaire reported on a series of 105 patients with average follow-up of 51 months (Lemaire, Skalli et al. 1997). The average age of the patients was 39.2 years (range 24 – 50 years). Fifty patients (48%) had undergone at least one operation. Clinical results were measured using a modified Stauffer-Coventry rating scale which scored low back pain occurrence, radicular pain occurrence, neurologic deficit, medication use, participation in daily living activities, work status preop and post op, and psychiatric status. Results were measured as relative gain (the authors stated, relative gain " = absolute gain/maximal gain minus preoperative score", where the assumption is that this is the same formula as in the 2005 Lemaire article, where relative gain is defined as post-operative score - preoperative score/maximum possible score – preoperative score).

Table 5.

Relative Gain	Result	Percentage of Patients
> 70%	Good	79
60% – 70%	Fair or Satisfactory	5.8
< 60%		15.2

Relative Gain	Result	Percentage of Patients
	Poor	

The authors attributed bad results to incorrect indications (osteoporosis, posterior osteoarthritis, over-lying thoracolumbar kyphosis), secondary progression of a posterior facet joint syndrome, or non-return to work. Eighty-seven percent of patients returned to work. Sixty percent had the same work activity, 27 % had reduced activity, and 13% did not return to work. Ten percent returned to "intense sports activities." Complications occurred in 11 patients (10%): 5 vascular problems (2 phlebitis, 2 pulmonary embolism, 1 acute leg ischemia); 2 temporary neurologic deficits (1 total regressive sexual disorder at 1 year, 1 paralysis at L5 with recovery after revision and fusion); and 4 cases of bone related complications (1 L5 endplate facture requiring revision with arthrodesis, 1 L5 endplate subsidence of osteoporotic origin, 2 periprosthetic ossifications). Only 3 of these complications were attributed to technique. The results were also analyzed anatomically, biomechanically, and kinematically from X-rays. The average L4-L5 mobility was 9.7 degrees flexion, 3 degrees extension, and 4 degrees lateral bending. At L5-S1 level, these values were 6 degrees, 3 degrees, and 3 degrees, respectively. Interestingly, there was a correlation between posterior joint pain and anterior positioning greater than or equal to 4mm. These authors concluded, "In fact, the proper indication for surgery is crucial for good results."

A 1999 study by Zeegers in the Netherlands reported on 2 year results for 50 prospectively studied patients that he had operated on (Zeegers, Bohnen et al. 1999). There was a 13% rate of permanent side-effects and/or complications, with 4% related to poor implantation technique. Seventy-five prosthesis were placed in 50 patients: 29 patients had one level insertion, 18 had two level insertion, and 3 patients had three prostheses inserted. Four patients were lost to follow-up (unclear how these patients were regarded). The mean age at the operation was 43 years (24 – 59 years). Mean duration of low back complaints was 10 years (range 1 – 35 years). Fifty-four percent had undergone previous surgery. Patients under 45 years of age were associated with a statistically significant better outcome (< 0.05). Seventy percent of the patients had a positive clinical result defined as a good or fair result from the Stauffer and Coventry criteria. Sixty-five percent (30/46) showed improvement of low back pain. Eighty-one percent returned to some work and 43% returned to their original work. Only fifteen out of 34 patients were able to decrease their analgesic intake. Twelve patients (24%) out of the fifty initial patients needed re-operation which involved 24 procedures (re-operation at the segment with a prosthesis: 6 ; re-operation at other levels: 11; re-operation related to complications: 7). Side-effects or complications at, or after, the first implantation operation were reported 52 times by 30 patients, with permanent sequela and complications seen in 13%. These included dysaesthesia of legs (3 permanent), painful/numb scar or hematoma (17 temporary), abdominal problems (3 temporary), new or progression of old pain (5 temporary), sympathectomy effect (4 permanent), aortic lesion at removal of prosthesis (temporary), general complication of urinary tract infection, impotence, deep venous thrombosis (5 temporary), malposition of prosthesis (one temporary and one permanent). Fourteen percent of all levels with a prosthesis showed a decrease in height 2 years after surgery. There was no significant migration (> 2mm). The range of motion of the prosthesis between flexion and extension averaged 9 degrees 2 years postoperatively, which equaled the preoperative ROM. The authors provided these comments, "A critical review of our good and poor clinical results makes clear how difficult it is to find the real origin of low back pain," and, "Several indications and contra-indications for ADR [artificial disc replacement] have been previously reported, but are not unanimously accepted."

A small case series study by Sott and Harrison in the UK attempted to study patients over 45 years of age (Sott, Harrison 2000). They mentioned that an upper age limit of 45 years was proposed by the manufacturers and several authors, "as increasing age may lead to weakening of the bone structure supporting the prosthesis." Fifteen prostheses were implanted into 14 patients aged 31 to 61 years (mean age 48 years). Nine prostheses were implanted at level L4/L5, four at L3/L4 and two at L5/S1. None of the patients were able to carry out their usual professional, domestic or leisure activities without pain preoperatively. The patients were followed for an average of 48 months (18 to 68 months). Four patients were followed up by phone. Criteria for clinical results were according to the Stauffer and Coventry classification. The patients were divided into two groups, those less than 45 years (7) and those over 45 years (7). Patient outcomes related to age were identical for both groups: 5/7 good, 1/7 fair, and 1/7 poor. There was one case of implant migration in a woman with normal bone density preoperatively. Another patient required fusion for symptoms related to a non-operated level.

A 2002 abstract by David reported on 147 patients implanted with the Charite prosthesis with a minimum of five years follow up (David 2002). Patients had 163 prosthesis implanted (16 at two levels) in L4-L5 and/or L5-S1 for chronic low back pain alone (59), or with sciatica (88). Seventy two patients had been operated on before. The results were stated as 79% of 142 patients had excellent or good results using the Stauffer Coventry classification. One patient had removal with fusion for severe sciatica, two had secondary bone migration with fusion and ten patients had fusion (prosthesis left in place) for malpositioning and facet pain. Eleven patients had partial or total ossifications around the prosthesis. The author concluded, "Good positioning of the implants is very important for long term mobility to avoid facets deterioration."

In 2003 a systematic review of case series studies was reported by de Kleuver (de Kleuver, Oner et al. 2003). This review included 6 of the 7 short term case series [246 patients] mentioned in this document (all except Caspi 2003), two foreign language articles [74 patients], and 6 Acroflex disc patients. The authors reported that patients classified as having "good" or "excellent" results varied in the studies from 50% to 81%. Various complications were observed in 3-50% of patients, including vascular injury, implant migration/subsidence, or dislocation. A meta-analysis could not be performed due to the lack of comparative studies. The authors concluded that there was insufficient data to assess the performance of total disc replacement.

In 2003, Caspi reported the outcome of 20 patients implanted with Charite SB III after a 48 month follow-up (Caspi, Levindopf et al. 2003). Preoperative diagnosis included degenerative diskopathy (DDD) in 17 patients and failed posterior conventional diskectomy in 3. Seventeen patients had one level implantation and 3 patients had two level implantation. Age range was 24 to 50 years. Three of 20 patients had undergone previous surgery by a posterior approach. The authors stated the results of these 20 patients as:

"The overall clinical results were rated as follows: fair = 3, good = 4, excellent = 11, and poor = 4 (one patient underwent secondary fusion and one is waiting for surgery). With regard to the patients' recovery in terms of occupation: four are completely disabled, one patient resumed physical labor, and the others returned to light and sedentary work."

There were two cases of migration of the prosthesis, one intraoperative laceration of the ureter and thrombosis of the iliac artery occurred. Two patients had ossification of the intervertebral anterior ligament. Average range of motion was given as 3 – 9 degrees. Though it was stated that radiologic results were analyzed from X-rays and that the clinical outcome was assessed by comparing presurgical with follow-up data using the Oswestry questionnaire and the visual pain analogue scale, no details were given as to how the statement of clinical results was arrived at. One of the conclusions of this article was, "Contraindications for surgery appear to be the principal cause for failure rather than the prosthesis itself."

In 2005, Lemaire reported on a 10 year minimum follow-up of 100 of 107 original patients (Lemaire, Carrier et al. 2005). They were followed for a minimum of 10 years (range 10 – 13.4 years). Seven patients were unavailable for long-term follow-up. Fifty-four patients were implanted with one-level, 45 were implanted with two-level, and one with three-level prostheses. Age at time of surgery was 39.6 years (range = 23.9 – 50.8 years). While the mean age and range were very close to the 1997 Lemaire study, the mix of male and female differed (1997 [68 M, 37 F], 2005 [41 M, 59 F]). Patient indications included DDD with low back pain of discogenic origin at one or two levels (one had three-level surgery) and failure of nonoperative treatment (PT, medication, exercise). Contraindications were obesity, prior fusion, instability, deformity, radicular pain symptomatology, and facet arthrosis. Radiographs, MRI (not in early cases), and provocative discography were done preoperatively. Clinical outcomes were determined using a modified Stauffer Coventry scoring system, as in the previous Lemaire, et al., 1997 study. The results were reported as relative gain in the modified Stauffer Coventry Scale, which was defined as post-operative score - preoperative score/maximum possible score – preoperative score, expressed as a percentage. A relative gain of at least 70% was defined as excellent (no pain, no medication, resumption of activity in the same job after 3 months), 60 – 69% as good (intermittent and infrequent lumbar pain not requiring major or prolonged medication, resumption of activity in the same job after > 3 months or in a less strenuous job after < 3 months) and less than 60% as poor. By this definition, 62% of patients had excellent results, 28% good results and 10% poor results. For the 95 patients who had not retired, 87 returned to work. There was no statistical difference in outcomes between patients with one level prosthesis versus two level ($p < 0.05$). Radiologic analysis was performed using anatomic, biomechanical and kinematic criteria. By radiologic evaluation, no subluxation of the prosthesis or the core was noted. Minor subsidence was noted in two patients, both due to trauma. Osteolysis was not identified. Sixteen of the 59 women were menopausal at the time of follow-up, with no radiologic signs of osteoporosis. Pelvic anteversion (increase of the sacral slope, reduction of the pelvic version) was noted as being "routinely obtained or preserved". Mean range of motion was reported as 10.3 degrees flexion/extension and 5.4 degrees lateral bending. Five patients (5%) had a secondary arthodesis, with two of the five reported as having good outcomes. Four had symptomatic articular arthritis. Two patients (3%) had periprosthetic ossification (bone formation adjacent to the prosthesis) affecting prosthesis mobility, which the authors compared to 7.7% in David's series (David 2002) and 1.7% in Marnay's series (Marnay 2002). They reported no correlation between ossification and outcomes. If the ossifications were lateral, the segment fused, if anterior, the segment was mobile. Lemaire, et al., stated, "Because these ossifications appear after the fifth year postoperatively, the risk of adjacent functional overload can appear as late as after the 15th year postoperatively." Two patients had adjacent level degeneration. The level of identified complications (9%) was reported as being equal to David's experience, and lower than Marnay's Prodisc series (26%).

In a 2005 article Putzier reported on clinical and radiographic results of 17 years from Charite – University Medicine in Berlin (Putzier, Funk et al. 2005). It was a study of 71 consecutive patients treated surgically with either Charite I, II, or III between 1984 and 1989 with 84 Charite disc implants. The follow-up averaged 17.3 years (14.5 – 19.2 years), and ultimately 53 patients (74.6%) were available for examination. There were 20 males and 33 females with an average age of 44 years (30 – 59 years). Treated levels included L3/4, L4/5, L5/S1, and L4-S1. Fifteen patients had type I, 22 patients had type II, and 16 had type III. Surgical indication was one or 2 segment DDD of the spine. Eight patients had had previous disc surgery, and 3 had spondylolisthesis grade I. All operations were performed by experienced senior spine surgeons and included the designers of the prosthesis. Clinical examination included the ODI and the VAS. The patient's perception of the overall outcome was graded at follow-up as excellent, good, fair, or poor according to Odom's criteria (a functional outcome scoring system). Radiological parameters included plain X-rays with flexion/extension views. A segmental mobility of 3 degrees or less was graded as fused, with more the 3 degrees graded as mobile. Adjacent segments were evaluated to determine any progression of degeneration in comparison to preexisting X-rays. Clinical results are as follows:

Oswestry disability index

Type I: mean 40.76 SD 19.64
Type II: mean 45.67 SD 22.45
Type III: mean 37.18 SD 22.12 **Visual analog scale**
Type I: mean 40.76 SD 19.64
Type II: mean 45.67 SD 22.45
Type III: mean 37.18 SD 22.12

Outcome criteria according to Odom, in relation to the type of prosthesis

	excellent	**good**	**fair**	**Poor**	**GPA***
Type I	27% (4)	27% (4)	33% (5)	13% (2)	2.33
Type II	23% (5)	32% (7)	13% (3)	32% (7)	2.55
Type III	31% (5)	27% (4)	33% (3)	13% (4)	2.38
*grade point average, with excellent grade 1, good grade 2, fair grade 3, poor grade 4.					

Upon statistical examination, there was no significant difference between the three types of Charite for all three clinical parameters. Radiological results revealed that of the 53 patients available for follow-up, 12 (23%) had surgical fusion. Of the remaining 41 patients, only 9 patients (17%) did not have heterotopic ossification of ankylosis.

	Classification of heterotopic ossification/fusion *				

	Classification of heterotopic ossification/fusion *				
Charite disc type	**0**	**I**	**II**	**III**	**IV**
I	0 (0%)	0 (0%)	0 (0%)	0 (0%)	12 (80%)
II	0 (0%)	0 (0%)	2 (9%)	1 (5%)	11 (50%)
III	1 (6%)	1 (6%)	2 (13%)	2 (13%)	9 (56%)
Total	1 (6%)	1 (2%)	4 (8%)	3 (6%)	32 (60%)
*Classification of heterotopic ossification/fusion according to McAfee					

Adjacent segments were evaluated for degenerative changes, with 9 cases having significant degenerative changes. The authors commented, "Adjacent segment alterations were found only in cases where spontaneous ankylosis of the treated segments, spondylodesis, or fusion after implant failure occurred." The different types of discs were not found to influence this (no statistical significance), nor did it matter if the ankylosis was spontaneous or there was surgical fusion. The authors also correlated clinical parameters with radiological results. Interestingly, the clinical parameters did not correlate with the radiologic evaluation of functional status of the surgically treated segment.

Table 6

Status of segmental Fusion	**Patients (n)**	**Oswestry disability index**		**Visual analog scale**		**Odom's Criteria**
		Mean	**Standard deviation**	**Mean**	**Standard Deviation**	**GPA**
No fusion	9	52.09	14.42	6.08	1.35	2.67
Spontaneous Ankylosis	32	37.84*	10.41	4.45*	1.14	2.34

Status of segmental Fusion	Patients (n)	Oswestry disability index		Visual analog scale		Odom's Criteria
		Mean	Standard deviation	Mean	Standard Deviation	GPA
Fusion after implant Failure	12	44.28	17.04	4.93	1.56	2.50
*p < 0.5 in comparison to "no fusion"						

Adverse Events

van Ooij, in 2003, reported on a series of 27 patients who presented to a tertiary care center with an unsatisfactory result or complication after Charite disc replacement (van Ooij, Oner et al. 2003). These patients, (except for one), belonged to a series of approximately 500 patients operated on in a single institution. The mean age was 40 years (range 30 – 67 years) at the time of operation. Presentation was at a mean of 53 months (range 11 – 127 months) following total disc replacement. Twenty-two patients had the prosthesis implanted at a single level, four patients received two disc implants, and one patient received three implants. Early complications included one patient who had a dislocated disc implant anteriorly within one week postoperatively, then had a subsequent fusion cage placed, and continued to have disabling back pain 2 years out. The 26 late complication patients were described as, "The clinical picture of most of the patients was of a very disabling nature." Patients often had a combination of pathologies. Degenerative disc disease at another level (either present before the operation or developed afterwards) was seen in 12 patients. Facet joint arthrosis (at the operated level or at a neighboring level) was seen in 11 patients. Subsidence was present in 18 patients. Two patients had migration of the prosthesis which resulted in compression on the great vessels in one patient. Breakdown of the polyethylene was seen in one patient.

Adverse events reported in the Manufacturer and User Facility Device Experience (MAUDE) database

The FDA provided an analysis of adverse events reported in MAUDE database at the request of CMS (FDA memorandum to CMS 2005). The analysis includes Medical Device Reports (MDRs) that were entered into the database between August 11, 2003 (date first report was received) and November 16, 2005. A total of 101 MDRs were analyzed for 96 patients, 1 MDR for the Prodisc device in addition to the Charite devices. The most frequently reported event was device migration out of the implanted location, with 54 of 96 patients (56%) experiencing this adverse effect. Seventy-six patients (79%) had a second surgery to remove all or part of the implant, to correct problems with the device, or to correct problems produced during the implant surgery. Fifty of the 76 (66%) patients had second surgery due to device migration. The most common second surgery was removal of all or part of the artificial disc followed by spinal fusion of the implanted motion segment. Twelve patients had two prostheses placed despite the device labeling for only one device implantation. Most adverse events that required second surgery occurred in the first 2 months after implantation. Two deaths were reported which were both attributed to pulmonary emboli.

4. Medicare Coverage Advisory Committee (MCAC) Meeting

The MCAC was not held for this topic.

5. Evidence-based guidelines

No evidence-based guidelines were identified.

6. Professional Society Position Statements

Five professional societies provided comment - the North American Spine Society, the Scoliosis Research Society, the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the Spine Arthroplasty Society. The North American Spine Society noted "…there have not been any published studies assessing the utilization of TDR [total disc replacement] in the elderly population" and "osteoporosis and osteopenia are direct contraindications for this device." They further noted "based on current science and clinical information we simply cannot determine whether or not TDR would be indicated in elderly patients." They expressed worry that non-coverage could stop the advancement of the TDR technology as well as influence third party payors. The Scoliosis Research Society stated "an extremely small minority of patients indicated for total disk arthroplasty fall within the CMS purview." The AANS/CNS (3 identical comments) stated "there is not enough available data on patients over the age of 60 to demonstrate that this procedure is inappropriate for elderly patients" and that "careful patient selection is essential and the surgeon, in consultation with the patient, is the best person to decide if his or her patient is a candidate for artificial disc surgery, regardless of the patient's age." AANS/CNS was also concerned about the impact of non-coverage on other payors.

Two leaders of the Spine Arthroplasty Society, an international society, offered comments, one from the president and the other from the first vice president. The first vice president of the Spine Arthroplasty Society, Dr. Hochschuler, stated "We do not believe CMS will have sufficient data available to them to make an informed decision, especially on patients 65 and older for which Medicare is responsible." He further stated "Today's older patients take better care of themselves and have more active lifestyles. These patients want restoration, and not fusion, in order to maintain their activities." The president of the Spine Arthroplasty Society, Dr Marnay, of France, stated, "Nearly 20,000 total disc implantations have been performed throughout the world. Studies under the regulatory control institutions have been conducted in several countries and preservation of motion devices got their approval after showing their effectiveness, safety and the quality of these results compared with the current treatment options (conservative, simple discectomy and fusion) in some of the indications defined by those studies and confirmed by the scientific community." Dr. Marnay went on to say:

"In all the total disc replacement scientific studies performed in the last 15 years in Europe and the United States, in the frame defined by the FDA for an IDE, the average of the patients operated on remains between 44 to 46 years of age. After age 65, the number of indications is very limited; including global lumbar spine degeneration, facet anatomical deformities and quality of the bone are the limiting factors. So this point cannot be a subject of debate.

However, the choice of this surgical treatment, Total Disc Replacement, if it is clinically and anatomically indicated, remains the decision of the surgeon according to all the other elements of the analysis, including but not limited to daily activity of the patient, global health, and bone density measurement. The type of disc prosthesis to be used according to the biomechanical situation is the last point to be decided at that moment. In the current indication defined in the majority of the cases operated on between ages 18 to 60, (average of the case mid 40s), the degenerative disc disease generates the use of medications for a lot of months, rehab therapy, cast and at the end an impossibility to go to work. …We want to remind that the global cost of the disc degenerative disease is the first point of expenses for health care in developed countries but has also a global cost on the production level as the first origin of non-worked days."

7. Comments

CMS requested public comment relating to the following issue: whether there is adequate evidence for evaluating health outcomes of the lumbar artificial intervertebral disc surgery in the Medicare population.

A total of one hundred and thirty-eight public comments were received. The comment sources included patients who had disc replacements or whose children had disc replacements (13), stakeholders including device manufacturers, and health care providers, the vast majority of whom were orthopedic surgeons and neurosurgeons involved in spine surgery. Fifty-seven of the respondents identified themselves as either providing disc replacement surgery or having been trained to provide disc replacement surgery.

The majority of comments received asked that CMS deny the request for non-coverage of the lumbar artificial disc. Though in this group there was agreement that the request should be denied, opinions varied on patient selection and whether there is adequate evidence for evaluating health outcomes of the lumbar disc arthroplasty in the Medicare population. Five physicians supported the non-coverage request.

A. Comments with Evidence

Twenty six articles were submitted as evidence (See Appendix C). Of these, eleven are not articles about the Charite lumbar artificial disc. Six are Charite clinical studies and are mentioned in this document. Two are early reports on the Charite clinical trial; the final study is mentioned in this document. Four of the articles have been reviewed but are concerned with Charite disc design, biomechanics, or surgical technique and do not present additional evidence of benefit to the Medicare population. One reference is a letter to the editor; one reference is in press; and one reference is a roundtable discussion and monograph through a restricted educational grant by DePuy Spine.

One commenter said, "While most surgeons agree that disc arthroplasty is not ideal for the elderly, recent articles in Asia have questioned this." A literature search did not identify these articles.

B. Comments without Evidence

Most respondents were in agreement to deny the request for non-coverage of the lumbar artificial disc. Other comments were offered on a variety of issues.

Some comments addressed whether there is adequate evidence for evaluating health outcomes of the lumbar artificial intervertebral disc surgery in the Medicare population. There was a suggestion to delay the decision due to lack of sufficient data (16 of 17 comments were from physicians). In contrast, fourteen physicians expressed the sentiment that most of the Medicare population would not be candidates, implying that there would not be data because this population is for the most part excluded on the basis of selection criteria.

Physicians who chose to comment on patient selection offered a wide range of possibilities, with no clear agreement. Physicians also commented on the clinical results of disc arthroplasty, the comparison of disc arthroplasty to fusion, and some expressed concerns related to the procedure. Other opinions were expressed addressing policy scope, future products and economic issues.

Public comment sometimes cites the published clinical evidence and gives CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under Title XVIII of the Social Security Act §1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." § 1862(a)(1)(A). This section presents the agency's evaluation of the evidence considered and conclusions reached for the assessment questions.

CMS focused on this general question:

Is the evidence sufficient to conclude that lumbar artificial disc replacement with the Charite lumbar artificial disc will improve net health benefits for low back pain due to degenerative disc disease in the Medicare population?

Identifying the cause for chronic low back pain is challenging due to the complexity of the spine and poorly understood neurophysiologic mechanisms of pain sensation (Haldeman 1999). For a variety of reasons, the damaged intervertebral disc (common in middle age and universal in old age) is judged to be the cause of chronic pain in many patients with low back pain (Huang, Sandhu 2004). A reliable test to determine the exact cause of low back symptoms has yet to be developed. Therefore, treatment of symptoms relies on clinical judgment. The majority of patients with low back pain will have acceptable results without surgery. In some patients, the pain is persistent and can eventually result in functional limitations. Spinal fusion surgery is offered to patients who do not respond to conservative treatments, though no universally accepted indication guideline exists. Improvement in short term pain and function from fusion is variable, and long term results are controversial. The artificial lumbar disc has been developed as an alternative to fusion, with the premise that segmental mobility will improve outcomes, as has been the case for artificial hip and knee replacements.

The earliest evidence for benefits and risks with the Charite lumbar artificial disc comes from case series studies. In the 2003 systematic review of case series studies, de Kleuver, et al., reported that patients classified as having "good" or "excellent" results varied in the studies from 50% to 81%. However, these numbers were difficult to interpret as there was no comparison group and no standardized method of reporting to compare study outcomes (de Kleuver, Oner et al. 2003). Various complications were observed in 3-50% of patients. Patients with poor outcomes are candidates for fusion, with or without removal of the implant; however, posterolateral fusion without removing the disc may give unsatisfactory results, and the repeat anterior spine approach is challenging even for the most skilled surgeons. The authors all seemed to agree that patient selection is very important, yet the question of who is most appropriate for the device remains unanswered from these studies. The disc has been promoted as an alternative to fusion; yet, even in these short term studies, spontaneous and surgical fusion occurred. As the disc will be required to function for many years, important information about longer term benefits and risks, such as satisfaction, adjacent segment problems, and rate of re-operations, could not be answered by these earlier studies.

The recent Charite randomized controlled trial was performed for the FDA Premarket Approval Application. However, as with other new products that go through this process, only short term results (24 month follow-up) are provided. While short term outcomes are important, strong consideration must be given to the fact that the device is designed to function for many years. The comparison group, Bagby and Kuslich (BAK) cages with iliac crest bone graft, may not be the current favored surgical fusion method, as other cages and techniques have shown a higher success rate and better ODI and VAS scores than either group in the Charite clinical study (Zindrick, Lorenz et al. 2005; Mirza 2005; Button, Gupta et al. 2005). What implications this has for health benefits in the context of a noninferiority trial is not clear, where the Charite disc has been shown to be noninferior to a device that has fallen out of favor in the clinical community due to unsatisfactory outcomes.

Clinical success in this trial was defined by four criteria: (1) more than 25% improvement in the Oswestry disability score at 24 months after surgery, (2) no device failure, (3) no major complication, and (4) and no neurologic deterioration. This composite outcome is unconvincing as a demonstration of net health benefit, particularly so when these points are also considered: 1) only 57% of disc replacement patients and 46% of BAK fusion patients met these four limited criteria; 2) in patients who were considered a clinical success at 24 months, 64% of the Charite group and 80.4% of the control were using narcotics; 3) at 24 months the change in VAS and ODI did not differ statistically from control; 4) the SF-36 PCS and MCS composite scores did not differ statistically from control; 5) no difference in operative time or blood loss between the two groups. The mean duration of hospitalization did differ (3.7 days versus 4.2 days for control) in these highly selected patients, but discharge criteria were not standardized. A point was made by investigators that patient satisfaction was greater in the disc group than the fusion group, yet those who entered the study were obviously willing to receive the new technology, and perhaps could have been disappointed with receiving the older technology (Zindrick, Lorenz et al. 2005). A summary of satisfaction of those who did not participate in the trial and subsequently had fusion, for response comparison purposes, was not presented, which would have made these results more convincing (Zindrick, Lorenz et al. 2005). Additionally, a sensitivity analysis was done with various imputations for patients that did not have complete follow-up data. The technique of data imputation by the sponsor was "last value carried forward." If data scenarios are examined to impute missing data, one finds that in a worst case scenario, where the missing data favored BAK fusion success and failure for Charite for the missing observations, noninferiority criteria were not met (FDA in-depth statistical review for expedited PMA 2004).

In specific consideration of the Medicare population (who are either elderly, disabled, or both), study exclusion criteria of the Charite randomized controlled trial limit the generalizability of results. For instance, no one over age 60 was included in the study and patients with osteoporosis, osteopenia, and metabolic bone disease were excluded. Data was not provided on how many patients were screened to arrive at the 375 enrolled. Patients eligible for the Charite disc implantation, using strict criteria, may be narrowly focused. A study by Huang found that of 100 consecutive patients who had lumbar surgery in one spine surgeon's practice, 95% of patients had one or more contraindications to disc replacement, with the mean number of contraindications of 2.5 per patient (Huang, Sandhu 2004).

The short-term adverse event data from the Charite randomized controlled trial are not easy to interpret. The publicly accessible FDA website does provide additional information. In the reporting of adverse events, some events are self-limited and resolve without incident, whereas other events may need additional services and may not easily resolve, creating significant morbidity. Patients may have more than one adverse event, a circumstance which is not differentiated in the reporting, so a straightforward calculation of rate may not have a clear meaning. Also in this study, there is a distinction between device related complications and approach related complications, which may not reflect the over-all risk for the procedure. It is valuable for patients to have an accurate perspective of risk.

The adverse effects noted in the analysis by the FDA are of potential concern. While a rate cannot be calculated without the total number implanted thus far, one can consider rates from other studies. Interestingly, most of these complications in the MAUDE database occurred within 2 months of operation. Bertagnoli noted:

“Most of the complications in total disc replacement procedures are iatrogenic; wrong indications, poor implantation technique, and improper positioning of the implant are the most likely causes. Isolated device-related complications are rare (e.g., subsidence, body fractures, polyethylene extrusion, and problems due to polyethylene wear). Due to stringently controlled inclusion groups, small study populations, and lack of long-term follow-up, only limited data are available. Lessons learned from hip and knee arthroplasty, however, suggest that the incidence of complications increases with duration of follow-up” (Bertagnoli, Zigler et al. 2005).

van Ooij raised interesting points in his case series report of complications with a mean follow-up of 53 months (van Ooij, Oner et al. 2003). He pointed out that while the disc prosthesis was often compared to hip and knee prosthesis, the multidimensional motion of the spinal segment is totally different than that of a hip or knee joint, so a comparison may have significant limitations. The normal intervertebral disc has a shock absorbing function, but very little has been written about this. In his series, they saw seven patients that had degeneration at levels other than the operated one, where it was not present before surgery. It is unclear if this is the result of the degenerative disease progressing, or, the result of stresses on the adjacent levels. van Ooij stated, “Many questions still exist concerning the biomechanics of a disc prosthesis.” Other important points he raised concerned the anterior surgical approach. The great vessels were mobilized for prosthesis insertion. The dimensions of the plate determined the extent of dissection. He acknowledged that this potentially could create bleeding and thromboembolic risks for the great vessels, which has been reported. Concern has been raised about the long term behavior of the biomaterials in the spine. Hallab, in his article on spinal implant debris-induced osteolysis, expressed a related concern, “With the introduction of modular artificial disc replacements and new materials for orthopedic spinal implants, the effects of implant debris on local and systemic tissues remains and will likely increase as a clinical concern ”(Hallab, Cunningham et al. 2003). If disc arthroplasty fails, there are three options: posterior fusion; revision replacement; and, anterior fusion (Kostuik 2004). As expressed by van Ooij, many agreed that revision through a repeat anterior lumbar approach can be very dangerous because of the adherence to the great vessels and the nerve plexus. While removal may not always be necessary in disc arthroplasty failure, some suggested posterior fusion may not give satisfactory results (van Ooij, Oner et al. 2003).

The 10 year follow-up study by Lemaire does give some evidence of long term viability (Lemaire, Carrier et al. 2005). It was unclear though, if follow-up was systematic or when the measures listed were recorded. The standard measures of VAS and ODI were not reported, and the Modified Stauffer Coventry scale score was not reported, but rather a percentage “relative gain”. Though complications were reported, it was not clear how many patients were free from complications at follow-up. There was no correlation of mobility with outcome. It was unclear how these case series patients differed from his 1997 fifty-one month case series study, as the mean age and range were very close, the mix of male and female differed (1997 [68 M, 37 F], 2005 [41 M, 59 F]), drawing into question who was included.

Putzier raised several important points in his 2005 article (Putzier, Funk et al. 2005). Of the 53 patients, 83% were either surgically fused or spontaneously ankylosed, with only 17% having near normal function of the spine. The authors did state that many causes for spontaneous fusions must be considered, including preservation of the anterior longitudinal ligament, which currently is believed to be a trigger for ossification. Secondly, they mentioned that for correct implantation of the prosthesis a complete removal of the remaining disc tissue must be accomplished, including decortication of the vertebral endplates. This process releases osteoinductive substances, which may also have caused this high rate of ossification. Additionally, they offered that “since all of the reported patients suffered preoperatively from moderate to severe DDD, a progression of these processes after surgery can be assumed.” An important point was that Charite I, II, and III are very different in design, yet there was no significant difference in the clinical or radiographic outcomes. One of the primary goals of the TDR is to prevent adjacent segment degeneration, yet the overall percentage judged radiographically (17%) was comparable to the results of follow-up studies after fusion surgery, which may follow from the high rate of spontaneous ankylosis. Lastly, those with preserved segmental mobility were statistically less satisfied than those with spontaneous ankylosis or surgical fusion. The authors hypothesized that while the anterior column is addressed by TDR, degenerative disorders of the posterior elements are not addressed.

Importantly, the major premise of spine segmental motion preservation is that adjacent level disease is increased by fusion surgery, and therefore that motion preservation will prevent this. However, there is no good evidence yet to support this premise, and there is some indication motion preservation with the Charite disc may not have an improved net health benefit. As Hassett reported in his study on ageing and the nonoperated lumbar spine, there was radiographic evidence of progressing osteoarthritis of 3% to 4% per year, without symptom correlation (Hassett, Hart et al. 2003). This rate has also been quoted as the risk of adjacent level disease after fusion.

Lastly, some patients with poor results from disc arthroplasty will require revision surgery. Revision with posterior fusion appears to give less than satisfactory results. Anterior fusion with required anterior reentry is challenging, as reflected in a comment by McAfee, "even the most experienced vascular access surgeon has difficulty with the formidable revision through a repeat anterior lumbar procedure" (McAfee 2004).

Conclusions

Important questions about the Charite lumbar artificial disc remain, principal among them are issues of patient selection, adverse events, and long term outcomes. Very few patients over the age of 65 have been treated with the Charite disc technology. Therefore, there is insufficient evidence for those over age 65 to determine net health benefit, with the suggestion that the Charite disc is not indicated in this population for a variety of reasons. The results of the Charite Premarket Approval noninferiority trial are unconvincing as a demonstration of net health benefit. The Charite studies without a comparison group make it difficult to draw clear conclusions on the benefit of treatment, though the studies do demonstrate adverse events (and some longer term outcomes) including spontaneous and surgical fusion, the result that the disc endeavors to avoid. Therefore, for the Medicare population who are not elderly, but who are under 65 and receive Social Security cash payments due to a disability and become eligible for Medicare after a two year waiting period, there is insufficient evidence for a net health benefit.

CMS is aware that there are several other disc technologies in FDA sponsored clinical trials in the United States. As previously stated, CMS is evaluating lumbar artificial disc replacement with a focus on the CHARITE Lumbar Disc in this analysis, since this was the only disc implant that had FDA approval at the time this proposed decision memorandum was ready for posting. However, we anticipate that when other lumbar spinal disc implants receive approval from the FDA that CMS will, by external request or internal direction, open this NCD for reconsideration with a thorough review of the evidence for each new disc implant. Since this NCD focuses on the Charite lumbar artificial disc, Medicare coverage under the investigational device exemption (IDE) for other lumbar artificial discs in eligible clinical trials is not impacted.

IX. Proposed Decision

The Centers for Medicare and Medicaid Services (CMS) proposes that the evidence is not adequate to conclude that the Charite lumbar artificial disc is reasonable and necessary. Therefore, we propose to issue a national noncoverage determination.

Appendices A & B[PDF, 76KB]

APPENDIX C

Articles submitted as evidence through public comments

1. Atlas SJ, Keller RB, Robson D, et al. Surgical and nonsurgical management of lumbar spinal stenosis: four-year outcomes from the Maine Lumbar Spine Study. Spine 2000; 25:556-562.

2. Atlas SJ, Keller RB, Wu YA, et al. Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the Maine Lumbar Spine Study. Spine 2005;30:927-935.

3. Blumenthal S, McAfee PC, Guyer RD, et al. A prospective, randomized, multicenter Food and Drug Administration investigational device exemptions study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion: part I: evaluation of clinical outcomes. Spine 2005;30:1565-1575.

4. Deyo RA, Ciol MA, Cherkin DC, et al. Lumbar spinal fusion. A cohort study of complications, reoperations, and resource use in the Medicare population. Spine 1993;18:1463-1470.

5. Deyo RA, Gray DT, Kreuter W, et al. United States trends in lumbar fusion surgery for degenerative conditions. Spine 2005;30:1441-1445.

6. Deyo RA, Nachemson A, Mirza SK. Spinal-fusion surgery - the case for restraint. N Engl J Med 2004;350:722-726.

7. Geisler FH. Surgical technique of lumbar artificial disc replacement with the Charite Artificial Disc. Neurosurgery 2005;56:46-57.

8. Geisler FH, Blumenthal SL, Guyer RD, et al. Neurological complications of lumbar artificial disc replacement and comparison of clinical results with those related to lumbar arthrodesis in the literature: results of a multicenter, prospective, randomized investigational device exemption study of Charite intervertebral disc. J Neurosurg Spine 2004;1:143-154.

9. Guyer RD, McAfee PC, Hochschuler SH, et al. Prospective randomized study of the Charite artificial disc: data from two investigational centers. Spine J 2004;4:252S-259S.

10. Hoffman RM, Wheeler KJ, Deyo RA. Surgery for herniated lumbar discs: a literature synthesis. J Gen Intern Med 1993;8:487-496.

11. Kent DL, Haynor DR, Larson EB, et al. Diagnosis of lumbar spinal stenosis in adults: a meta analysis of the accuracy of CT, MR, and myelography. AJR Am J Roentgenol 1992;158:1135-1144.

12. Link HD. History, design and biomechanics of the LINK SB Charite artificial disc. Eur Spine J 2002;11 Suppl 2:S98-S105.

13. Malter AD, McNeney B, Loeser JD, et al. 5-year reoperation rates after different types of lumbar spine surgery. Spine 1998;23:814-820.

14. McAfee PC, Cunningham B, Holsapple G, et al. A prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion: part II: evaluation of radiographic outcomes and correlation of surgical technique accuracy with clinical outcomes. Spine 2005;30:1576-1583.

15. McAfee PC, Fedder IL, Saiedy S, et al. SB Charite Disc Replacement: Report of 60 Prospective Randomized Cases in a U.S. Center. Spine 2003;28 Suppl:424-433.

16. Regan JJ. Clinical results of charite lumbar total disc replacement. Orthop Clin North Am 2005;36:323-340.

17. Turner JA, Ersek M, Herron L, et al. Surgery for lumbar spinal stenosis. Attempted meta-analysis of the literature. Spine 1992;17:1-8.

18. Turner JA, Ersek M, Herron L, et al. Patient outcomes after lumbar spinal fusions. JAMA 1992;268:907-911.

19. van Ooij A, Oner FC, Verbout AJ. Complications of artificial disc replacement: a report of 27 patients with the SB Charite disc. J Spinal Disord Tech 2003;16:369-383.

20. McAfee PC, Geisler FH, Saiedy S. The revisability of the Charite artificial disc replacement – analysis of 688 patients enrolled in the US IDE study of the Charite artificial disc. Spine: in press.

21. McAfee PC, Geisler FH, Scott-Young M eds. Roundtables in Spine Surgery: Complications and revision strategies in lumbar spine arthroplasty. St. Louis: Quality Medical Publishing, 2005. (roundtable discussion and monograph through a restricted educational grant by DePuy Spine).

22. Lemaire JP, Carrier H, Sari Ali E, et al. Clinical and radiological outcomes with the Charite artificial disc: a 10-year minimum follow-up. J Spinal Disord 2005;18:353-59.

23. McAfee, P. Letter to the editor. J Spinal Disorder Tech 2005;18:116-117.

24. Delamarter RB, Fribourg DM, Kanim LE, et al. ProDisc artificial total lumbar disc replacement: introduction and early results from the United States clinical trial. Spine 2003:28:S167-75.

25. Cunningham BW, Gordon JD, Dmitriev AE, et al. Biomechanical evaluation of total disc replacement arthroplasty: an in vitro human cadaveric model. Spine 2003;28:S110-7.

26. Cinotti G, David T, Postacchini F. Results of disc prosthesis after a minimum follow-up period of 2 years. Spine 1996;21:995-1000.

Back to Top

Bibliography

Anderson P, Rouleau J. Intervertebral disc arthroplasty. Spine, 2004;29:2779-2786.

Bao QB, McCullen GM, Higham PA, et al. The artificial disc: theory, design and materials. Biomaterials 1996; 17 (12):1157-67.

Bertagnoli R, Karg A, Voigt S. Lumbar partial disc replacement. Orthop Clin North Am 2005; 36 (3):341-7.

Bertagnoli R, Kumar S. Indications for full prosthetic disc arthroplasty: a correlation of clinical outcome against a variety of indications. Eur Spine J 2002;11:S131-S136.

Bertagnoli R, Zigler J, Karg A, et al. Complications and strategies for revision surgery in total disc replacement. Orthop Clin N Am 2005;36:389-395.

Blue Cross and Blue Shield technology assessment. Artificial vertebral disc replacement April 2005.

Blumenthal S, McAfee P, Guyer R, et al. A prospective, randomized, multicenter food and drug administration investigational device exemptions study of lumbar total disc replacement with the Charite artificial disc versus lumbar fusion. Part I: evaluation of clinical outcomes. Spine 2005;30:1565-1575.

Boden D, Davis D, Dina T, et al. Abnormal magnetic resonance scans of the lumbar spine in asymptomatic subjects. JBone Joint Surg 1990;72-A:403-8.

Button G, Gupta M, Barrett C, et al. Three- to six- year follow-up of stand-alone BAK cages implanted by a single surgeon. Spine J 2005;5:155-160.

Caspi I, Levindopf M, Nerubay J. Results of lumbar disk prosthesis after a follow-up period of 48 months. IMAJ 2003;5:9-11.

Chang BS, Brown PR, Sieber A, et al. Evaluation of the biological response of wear debris. Spine J 2004; 4 (6 Suppl):239S-44S.

Cinotti G, David T, Postacchini F. Results of disc prosthesis after a minimum follow-up period of 2 years. Spine 1996;21:995-1000.

Cohen SP, Larkin TM, Barna SA, et al. Lumbar discography: a comprehensive review of outcome studies, diagnostic accuracy, and principles. Reg Anesth Pain Med 2005; 30 (2):163-83.

Cunningham BW, Gordon JD, Dmitriev AE, et al. Biomechanical evaluation of total disc replacement arthroplasty: an in vitro human cadaveric model. Spine 2003; 28 (20):S110-7.

David T. Lumbar disc prosthesis: five year follow-up study on 147 patients with 163 SB Charite prosthesis. Eur Spine J 2002; 11(suppl 1):S18.

de Kleuver M, Oner F, Jacobs W. Total disc replacement for chronic low back pain: background and a systematic review of the literature. Eur Spine J 2003;12:108-116.

Delamarter RB, Bae HW, Pradhan BB. Clinical results of ProDisc-II lumbar total disc replacement: report from the United States clinical trial. Orthop Clin North Am 2005; 36 (3):301-13.

Diwan AD, Parvataneni HK, Khan SN, et al. Current concepts in intervertebral disc restoration. Orthop Clin North Am 2000; 31 (3):453-64.

Durbhakula MM, Ghiselli G. Cervical total disc replacement, part I: rationale, biomechanics, and implant types. Orthop Clin North Am 2005; 36 (3):349-54.

Enker P, Steffee A, McMillin C, et al. Artificial disc replacement: preliminary report with a 3-year minimum follow-up. Spine 1993;18:1061–1070.

Errico TJ. Lumbar disc arthroplasty. Clinical orthopaedics and related research 2005;435:106-117.

FDA guidance document for the preparation of IDEs for spinal systems. January 13, 2000. http://www.fda.gov/cdrh/ode/87.pdf. Accessed 1-6-06.

FDA In-depth Statistical review for expedited PMA (P040006) Charite artificial disc, DePuy Spine, Inc. (Dated Feb. 23, 2004) <http://www.fda.gov/ohrms/dockets/ac/04/briefing/4049b1_04_Statistical%20Review%20Memo%20JCC.pdf. Accessed 12-05-2005.

FDA Center for Devices and Radiological Health, Orthopedics and Rehabilitation Devices Panel Meeting, Friday September 9, 2005. http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4181t2.DOC . Accessed 2-02-2006.

FDA memorandum to CMS. Analysis of adverse events reported to MAUDE for the Charite artificial disc prosthesis. November 23, 2005.

FDA PMA memorandum. Clinical review 2004. http://www.fda.gov/ohrms/dockets/ac/04/briefing/4049b1_03_Clinical%20Review%20Memo%20MAY.htm. Accessed 12-05-2005.

FDA Summary of Safety and Effectiveness Data. 2004. http://www.fda.gov/cdrh/PDF4/p040006b.pdf. Accessed 12-05-2005.

Geisler F, Blumenthal S, Guyer R, et al. Neurological complications of lumbar artificial disc replacement and comparison of clinical results with those related to lumbar arthrodesis in the literature: results of a multicenter, prospective, randomized investigational device exemption study of Charite intervertebral disc. J Neurosurg (Spine 2) 2004;1:143-154.

Geisler F. Surgical technique of lumbar artificial disc replacement with the Charite Artificial Disc. Neurosurgery 2005; 56 (1 Suppl):46-57; discussion 46-57.

Gibson JNA, Waddell G. Surgery for degenerative lumbar spondylosis. The Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD001352.pub2. DOI:10.1002/14651858.CD001352.pub2.

Goffin J, Van Calenbergh F, van Loon J, et al. Intermediate follow-up after treatment of degenerative disc disease with the Bryan Cervical Disc Prosthesis: single-level and bi-level. Spine 2003; 28 (24):2673-8.

Griffith SL, Shelokov AP, Buttner-Janz K, et al. A multicenter retrospective study of the clinical results of the LINK SB Charite intervertebral prosthesis. The initial European experience. Spine 1994;19:1852-1849.

Gunzburg R, Mayer HM, Szpalski M, et al. Arthroplasty of the spine: the long quest for mobility. Eur Spine J 2002;11:S63-S64.

Haldeman S. Low back pain. Current physiologic concepts. Neurol Clin 1999;17:1-15.

Hallab N, Cunningham B, Jacobs J. Spinal implant debris-induced osteolysis. Spine 2003:28;S125-S138.

Hassett G, Hart DJ, Manek N, et al. Risk factors for progression of lumbar spine disc degeneration: The Chingford Study. Arthrit Rheum 2003;48:3112-7.

Hilibrand AS, Robbins M. Adjacent segment degeneration and adjacent segment disease: the consequences of spinal fusion? Spine J 2004; 4 (6 Suppl):190S-4S.

Hirsch C, Ingelmark BE, Miller M. The anatomical basis for low back pain. Studies on the presence of sensory nerve endings in ligamentous, capsular and intervertebral disc structures in the human lumbar spine. Acta Orthop Scand 1963; 33:1-17.

Huang R, Sandhu H. The current status of lumbar total disc replacement. Orhop Clin N Am 2004;35: 33-42.

Huang RC, Girardi FP, Cammisa FP, Jr., et al. The implications of constraint in lumbar total disc replacement. J Spinal Disord Tech 2003; 16 (4):412-7.

Kostuik J. Point of View. Spine 1996;32:1000.

Kostuik JP. Complications and surgical revision for failed disc arthroplasty. Spine J 2004;4:289S-291S.

Krismer M. Fusion of the lumbar spine. A consideration of the indications. J Bone Joint Surg (Br.) 2002;84:783-794.

LeHuec JC, Mathews H, Basso Y, et al. Clinical results of Maverick lumbar total disc replacement: two-year prospective follow-up. Orthop Clin North Am 2005; 36 (3):315-22.

Lee CK, Langrana NA. A review of spinal fusion for degenerative disc disease: need for alternative treatment approach of disc arthroplasty? Spine J 2004; 4 (6 Suppl):173S-6S.

LeHuec JC, Kiaer T, Friesem T, et al. Shock absorption in lumbar disc prosthesis: a preliminary mechanical study. J Spinal Disord Tech 2003; 16 (4):346-51.

Lemaire J, Carrier H, Ali E, et al. Clinical and radiological outcomes with the Charite artificial disc. J Spinal Disord Tech 2005;18:353-359.

Lemaire J, Skalli W, Lavaste F, et al. Intervertebral disc prosthesis: results and prospects for the year 2000. Clin Orthop 1997;337:64-76.

Link HD. History, design and biomechanics of the LINK SB Charite artificial disc. Eur Spine J 2002; 11 Suppl 2:S98-S105.

Manek NJ, MacGregor AJ. Epidemiology of back disorders: prevalence, risk factors, and prognosis. Curr Opin Rheumatol 2005;17:134-140.

Marnay T. Lumbar disc replacement, 7-11 years results with Prodisc. Eur Spine J 2002; 11(suppl 1):S19.

Mayer HM, Korge A. Non-fusion technology in degenerative lumbar spinal disorders: facts, questions, challenges. Eur Spine J 2002a; 11 Suppl 2:S85-91.

Mayer HM, Wiechert K, Korge A, et al. Minimally invasive total disc replacement: surgical technique and preliminary clinical results. Eur Spine J 2002b; 11 Suppl 2:S124-30.

Mayer HM. Total lumbar disc replacement. J Bone Joint Surg Br 2005; 87 (8):1029-37.

McAfee P, Cunningham B, Holsapple G, et al. A prospective, randomized, multicenter food and drug administration investigational device exemptions study of lumbar total disc replacement with the Charite artificial disc versus lumbar fusion. Part II: evaluation of radiographic outcomes and correlation of surgical technique accuracy with clinical outcomes. Spine 2005;30:1576-1583.

McAfee PC. The indications for lumbar and cervical disc replacement. Spine J 2004:4:177S-181S.

McAfee PC. Comments on the van Ooij article. J Spinal Disord Tech 2005; 18 (1):116-7.

Mirza S. Point of view: commentary on the research reports that led to Food and Drug Administration approval of an artificial disc. Spine 2005;14:1561-64.

National Institute for Clinical Excellence. Interventional procedures consultation document - prosthetic intervertebral disc replacement. 2003. London. http://www.nice.org.uk/page.aspx?o=87531. Accessed 12-05-2005.

National Institute for Clinical Excellence. Overview of Prosthetic Intervertebral Disc Replacement, 2003. London. http://www.nice.org.uk/pdf/ip/ip126overview.pdf . Accessed 12-05-2005.

Oskouian RJ, Whitehill R, Samii A, et al. The future of spinal arthroplasty: a biomaterial perspective. Neurosurg Focus 2004; 17 (3):E2.

Polly DW, Jr. Adapting innovative motion-preserving technology to spinal surgical practice: what should we expect to happen? Spine 2003; 28 (20):S104-9.

Pope M, DeVockt, J. The clinical relevance of biomechanics. Neurol clinics North Am, 1999;17:17-41.

Putzier M, Funk J, Schneider S, et al. Charite total disc replacement – clinical and radiographical results after an average follow-up of 17 years. Eur Spine J 2005: published online October 28.

Regan J. Clinical results of Charite lumbar total disc replacement. Orthop Clin North Am 2005:36:323-340.

Salovey P, Seiber WJ, Smith AF, et al. Reporting chronic pain episodes on health surveys. National Center for Health Statistics. Vital Health Stat 6(6). 1992. http://www.cdc.gov/nchs/data/series/sr_06/sr06_006.pdf. Accessed 11/07/2005.

Santos E, Polly D, Mehbod A, et al. Disc arthroplasty: lessons learned from total joint arthroplasty. Spin JH 2004:4:182S-189S.

Shuff C, An HS. Artificial disc replacement: the new solution for discogenic low back pain? Am J Orthop 2005; 34 (1):8-12.

Singh K, Vaccaro A, Albert T. Assessing the potential impact of total disc arthroplasty on surgeon practice patterns in North America. Spine J 2004;4:195S-201S.

Sott AH, Harrison DJ. Increasing age does not affect good outcome after lumbar disc replacement. International Orthopedics (SICOT) 2000;24:50-53.

U.S. Department of Health and Human and Human Services. Vital and health statistics, Series 6: Cognition and survey management No.6. 1992. http://www.cdc.gov/nchs/data/series/sr_06/sr06_006.pdf. Accessed 11/07/2005.

U.S. Preventive Services Task Force. Guide to clinical preventive services, 2nd ed. Baltimore: Williams & Wilkins, 1996: 699.

van Ooij A, Oner F, Verbout A. Complications of artificial disc replacement; A report of 27 patients with the SB Charite disc. J Spinal Disorders & Techniques 2003:16:369-383.

Zeegers W, Bohnen L, Laaper M, et al. Artificial disc replacement with the modular type SB Charite III: 2-year results in 50 prospectively studied patients. Eur Spine J 1999;8:210-217.

Zigler JE. Clinical results with ProDisc: European experience and U.S. investigation device exemption study. Spine 2003; 28 (20):S163-6.

Zigler JE. Lumbar spine arthroplasty using the ProDisc II. Spine J 2004; 4 (6 Suppl):260S-7S.

Zindrick M, Lorenz M, Bunch W. Editorial response to Parts 1 and 2 of the FDA IDE study of lumbar total disc replacement with the Charite artificial disc vs. lumbar fusion. Spine 2005;30:E388-E390.

Back to Top